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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/545,072 04/07/00 LIN

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HM22/0727

EXAMINER

KUBELIK, A

ART UNIT

PAPER NUMBER

1638

DATE MAILED:

07/27/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<b>Office Action Summary</b>	Applicant(s)	LIN ET AL.	
	Examiner	Art Unit	
	09/545,072	1638	
	Anne Kubelik		

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 June 2001.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) 14 and 27-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13 and 15-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                     | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                            | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>5, 9</u> . | 6) <input type="checkbox"/> Other: _____                                    |

y.v.

### **DETAILED ACTION**

1. Applicant's election without traverse of Group I (claims 1-13 and 15-22) in Paper No. 11 is acknowledged.
2. A search for Group I recovered art applicable to Group III. Accordingly, as a courtesy to Applicant, Group III (claims 23-26) is rejoined to Group I, and claims 1-13 and 15-26 are examined. Claims 14 and 27-39 are withdrawn from consideration.

### ***Specification***

3. The title of the invention is not descriptive of the instant invention. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.
4. The abstract of the disclosure is objected to because it is not fully descriptive of the invention as claimed. Correction is required. See MPEP § 608.01(b).
5. The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. Applicant is required to delete all embedded hyperlinks and/or other forms of browser-executable code. See MPEP § 608.01.

### ***Claim Objections***

6. Applicant is advised that should claim 2 be found allowable, claim 9 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight

Art Unit: 1638

difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

***Claim Rejections - 35 USC § 101***

7. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claim 12 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is drawn to a plant comprising a nucleic acid encoding an SSE polypeptide, which reads on a product of nature.

The plant, as claimed, has the same characteristics and utility as those found naturally or as cellular precursors thereof and therefore does not constitute patentable subject matter. See *American Wood v. Fiber Disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). It is suggested that the claim be modified to refer to the hand of the inventor, *e.g.* by replacing “comprising” with --transformed with--.

***Claim Rejections - 35 USC § 112***

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-13 and 15-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids that encode SEQ ID NO:2, does not

Art Unit: 1638

reasonably provide enablement for nucleic acids that encode SSE proteins with 30% identity to SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a multitude of nucleic acids that encode SSE proteins with 30% identity to SEQ ID NO:2 and cells and plants transformed with those nucleic acids. The instant specification, however, fails to provide guidance for which amino acids of SEQ ID NO:2 can be altered to which other amino acids, and which amino acids must not be changed, to maintain the same activity of as that of SEQ ID NO:2. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional protein.

It cannot be predicted by one of skill in the art that nucleic acids that encode proteins with 30% identity to SEQ ID NO:2 will retain the same activity as the protein of SEQ ID NO:2. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to

Art Unit: 1638

the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252), who teach that a replacement of aspartic acid at position 47 with alanine or asparagine in transforming growth factor alpha had no effect, but that replacement with serine or glutamic acid sharply reduced biological activity (see the abstract). Small changes in amino acid sequence can completely modify enzymatic function; Broun et al (1998, Science 282:1315-1317) teach that a change of four amino acids converts an oleate 12-desaturase to a hydroxylase. Thus, Lazar et al and Broun et al demonstrated that one or few amino acid substitutions could dramatically affect the biological activity and the structure-function characteristics of a protein.

Even making “conservative” substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (*supra*) showed that the “conservative” substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while “nonconservative” substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the “nonconservative” amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the “conservative” amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins, however, would have much more than 30% identity to the original protein.

Art Unit: 1638

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids that encode SSE proteins with 30% identity to SEQ ID NO:2 and cells and plants transformed with those nucleic acids.

11. Claims 23-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn to any plant transformed with a construct that expresses an antisense SSE RNA from any source, and a construct to be used to produce that plant. The instant specification, however, fails to provide guidance for expression of a gene encoding an antisense SSE RNA from any source in any plant species.

Constructing an antisense RNA sequence that reliably inhibits gene expression is an unpredictable science. Arndt et al (1997, *Genome* 40:785-797) teach that the ability of an antisense construct to inhibit RNA expression is dependent on the rate of transcription of the antisense RNA relative to that of the sense RNA, the localization of the antisense gene in the genome, and the length of complementarity between the sense and antisense RNA; in addition, the effect of the latter varies from gene to gene and organism to organism (pg 787, left column). It can not be predicted which portion of a gene will work in antisense suppression of enzyme activity. An antisense RNA made to the 3' half of the chalcone synthase cDNA worked, while one made to the 5' half did not (van der Krol et al, 1990, *Plant Mol. Biol.* 14:457-466; see pg 459, right column, to pg 461, left column); however, in other systems, the 5' half of a gene has been effective (Bird et al, 1991, *Bio/Technol.* 9:635-639, see pg 636, left column, paragraph 1,

Art Unit: 1638

and Table 1) and the 3' end has not worked (Kuipers et al, 1995, Mol. Gen. Genet. 246:745-755, see pg 747, right column, last paragraph).

Antisense constructs that are not completely homologous can have very unpredictable effects. Colliver et al (1997, Plant Mol. Biol. 35:509-522) showed that transformation of bird's foot trefoil with a construct that was antisense to bean chalcone synthase resulted in transformants with *increased* levels of chalcone synthase transcripts (pg 519, left column, paragraph 2) and note other instances when this phenomenon has occurred (pg 519, right column, paragraph 1).

Plants of different species in which the expression of the same gene is inhibited via antisense constructs can behave very differently. While tomatoes containing an antisense acid invertase DNA construct grew identically to control plants (Klann et al, 1996, Plant Physiol. 112:1321-1330; see the abstract and pg 1323, right column, paragraph 1), carrot development is drastically altered when acid invertase expression is reduced via an antisense construct (Tang et al, 1999, Plant Cell 11:177-189; see pg 179, left column, paragraphs 1-2, and pg 184, left column, paragraph 1).

Lastly, antisense expression of genes encoding SSE polypeptides is also unpredictable. Leborgne-Castel et al (March, 1999, Plant Cell 11:459-469) teach that antisense inhibition of the gene encoding the SSE polypeptide BiP did not significantly decrease levels of BiP, presumably because decreased levels of the protein were lethal (pg 461, left column).

As the specification does not describe the transformation of any plant with a gene encoding the SSE polypeptide of SEQ ID NO:2 or any other SSE polypeptide, the unpredictability associated with antisense expression has not been overcome.



Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate plants of any species transformed with a construct that expresses an antisense SSE RNA from any source.

12. Claims 1-13 and 15-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of DNA molecules that encode an SSE polypeptide with 30% sequence similarity to SEQ ID NO:2 due to the deletion, insertion or substitution of an unspecified number of amino acids and to DNA molecules that encode any SSE polypeptide. In contrast, the specification only describes a coding sequence from *Arabidopsis* that comprises SEQ ID NO:1.

Neither the claims nor the specification provide a description of a unique function of the encoded protein. In the literature, "SSE polypeptide" describes proteins of a variety of functions, including the *shrunk seed 1* protein (Lin et al, 1999, Science 284, 328-330) and a heat-shock protein family (Storozhenko et al, 1996, FEBS Lett. 390:113-118).

The definition of SSE gene on pg 8 of the specification as one that encodes a polypeptide that governs or regulates protein and oil body biogenesis is not specific. The nature of the regulation is not defined, and therefore may include proteins that turn on transcription, proteins that turn off transcription, proteins that prevent translation, proteins that are involved in protein folding, proteins that are involved in membrane transport, or proteins that have any of a number

Art Unit: 1638

of other functions. Additionally, many different proteins perform each of those functions, and even describing a protein as one involved in transport is not specific. Thus, a single descriptive function of the SSE polypeptide has not been provided.

Hence, Applicant has not, in fact, described an SSE polypeptide, and therefore cannot describe any DNA molecule that encodes such a polypeptide. The specification fails to provide an adequate written description of the invention within the full scope of the claims.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997), where it states:

The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1-13 and 15-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

Claims 1-9 and 23 are indefinite in their recitation of the abbreviation "SSE." It is not clear to what "SSE" refers as the abbreviation is used in the literature for more than one kind of

Art Unit: 1638

protein and is described in the specification as more than one kind of potential protein activity.

Dependent claims are included in the rejection.

For clarity, the plant of claim 16 should be --transformed with-- the isolated nucleic acid, rather than “comprise” it. It is unclear whether the plant was transformed with the nucleic acid of claim 1 or 8 or if it was transformed with another nucleic acid.

Claim 8 is indefinite for its recitation of “hybridizes specifically” as the stringency of that hybridization is not specified.

### ***Claim Rejections - 35 USC § 102***

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 12-13, 16-19 and 21-22 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Akama et al (1992, Plant Cell Rep. 12:7-11).

Akama et al teach transformed *Arabidopsis* plants, cells and seeds (pg 8). These plants, cells and seeds would inherently comprise a nucleic acid encoding an SSE polypeptide.

17. Claims 1, 7 and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Mukai et al (1993, Gene 132:57-66).

Art Unit: 1638

Mukai et al teach two isolated nucleic acids encoding SSE polypeptides (Fig. 1). These nucleic acids would be in expression vectors and a bacterial cell for purposes of molecular biological manipulation.

18. Claims 1-5, 7-9 and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Storozhenko et al (1996, FEBS Lett. 390:113-118).

Storozhenko et al teach a cDNA from *Arabidopsis* that encodes an SSE polypeptide (pg 114-116). This cDNA would be in an expression vector and a bacterial cell for purposes of molecular biological manipulation and would hybridize under low stringency to SEQ ID NO:1.

Because heat shock proteins are involved in so many critical functions in the cell, including *protein binding and* maintenance of the endoplasmic reticulum (pg 113, left column, paragraph 2), this nucleic acid, when expressed in a cell of a plant, would facilitate intracellular transport of storage protein and the formation of *bodies* "food storage reserves."

19. Claims 1-12 are rejected under 35 U.S.C. 102(a) as being anticipated by Rounsley et al (February, 1999, GenBank Accession Numbers T00882 and F84893).

Rounsley et al teach a nucleic acid from *Arabidopsis* that encodes an SSE polypeptide. This nucleic acid has 96.9% homology to SEQ ID NO:2 (see sequence search results) and would be in an expression vector and a bacterial cell for purposes of molecular biological manipulation.

20. Claims 1, 3-6, 10-13, 15-18 and 21-26 are rejected under 35 U.S.C. 102(a) as being anticipated by Leborgne-Castel et al (March, 1999, Plant Cell 11:459-469) in light of Galili et al (1998, Plant Mol. Biol. 38:1-29).

Leborgne-Castel et al teach tobacco plants transformed with sense and antisense gene constructs encoding BiP; the plants were transformed by *Agrobacterium* (paragraph spanning

Art Unit: 1638

the columns on pg 460, Fig. 1; pg 461, left column; and pg 467, left column). Galili et al teach that BiP is involved in protein translocation into the ER and that proteins transported into the ER form protein and oil bodies (pg 3, right column; pg 17, left column, paragraph 1; and paragraph spanning pg 20-21). Therefore by the definition of an SSE polypeptide on pg 8, lines 25-26 of the instant specification, BiP is an SSE polypeptide.

21. Claims 1, 3-7, 10-13, 15-19 and 21-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al (1996, Mol. Gen. Genet. 252:11-19).

Lee et al teach transformation of *Arabidopsis* with a Hsp70 cDNA in an antisense orientation, and its effect on expression of the HSP70 and HSC70 genes (pg 12, right column, paragraphs 1-2; pg 13, left column, last paragraph, to pg 14). Galili et al teach that HSP70 is involved in protein translocation into the ER and that proteins transported into the ER form protein and oil bodies (pg 3, right column; pg 17, left column, paragraph 1; and paragraph spanning pg 20-21; see also Lee et al, pg 12, left column, 1<sup>st</sup> full paragraph). Therefore by the definition of an SSE polypeptide on pg 8, lines 25-26 of the instant specification, Hsp70 is an SSE polypeptide.

### ***Claim Rejections - 35 USC § 103***

22. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

23. Claims 1, 3-7, 10-13 and 15-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al (*supra*) in view of Dietrich et al (1991, Plant Physiol. 96:1268-1276), further in view of Gordon-Kamm et al (1990, Plant Cell 2:603-618).

The claims are drawn to monocots transformed with a gene encoding an SSE polypeptide.

Lee et al teach transformation of *Arabidopsis* with a Hsp70 cDNA in an antisense orientation, and its effect on expression of the HSP70 and HSC70 genes (pg 12, right column, paragraphs 1-2; pg 13, left column, last paragraph, to pg 14). Lee et al do not disclose maize plants transformed with that gene.

Dietrich et al teach a gene encoding a heat shock protein from maize (Fig. 4).

Gordon-Kamm et al teach transformation of maize and regeneration into plants.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to transform *Arabidopsis* with antisense constructs encoding the SSE polypeptide Hsp70 as taught by Lee et al, and to modify that to transform a construct encoding the maize heat shock protein described in Dietrich et al into maize plants as taught by Gordon-Kamm et al. One of ordinary skill in the art would have been motivated to do so because antisense expression in a plant species of a gene from that species is a common method for further understanding the mechanisms of action of heat shock protein genes.

24. Claims 1-13, 15-19 and 21-26 rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al (*supra*) in view of Storozhenko et al (*supra*).

The claims are drawn to cells and plants transformed with nucleic acids that encode an SSE polypeptide, including nucleic acids that produce antisense RNA.

Lee et al teach transformation of *Arabidopsis* with a Hsp70 cDNA in an antisense orientation, and its effect on expression of the HSP70 and HSC70 genes (pg 12, right column, paragraphs 1-2; pg 13, left column, last paragraph, to pg 14). Lee et al do not disclose genes encoding other SSE polypeptides.

Storozhenko et al teach a cDNA from *Arabidopsis* that encodes a different SSE polypeptide (paragraph spanning the columns on pg 113, and pg 114-116).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to transform *Arabidopsis* with antisense genes encoding the SSE polypeptide Hsp70 as taught by Lee et al, and to modify that to transform the plants with the SSE polypeptide gene described by Storozhenko et al. One of ordinary skill in the art would have been motivated to do so because the transformation of a plant with a sense or an antisense gene from that plant provides the most detailed elucidation of the role of that gene in the plant.

### Conclusion

25. No claim is allowed.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached on Monday through Friday, 8:15 am - 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula K. Hutzell, can be reached on (703) 308-4310. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne R. Kubelik, Ph.D.  
July 25, 2001

DAVID T. FOX  
PRIMARY EXAMINER  
GROUP 180-1638

*David T. Fox*